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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/001,267	10/31/2001	Lakshmi Rambhatla	093/004P	1874

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EXAMINER	
TON, THAIAN N	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 03/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/001,267	RAMBHATLA ET AL.	
	Examiner	Art Unit	
	Thai-An N Ton	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10/01,3/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants' Preliminary Amendment, filed 3/4/02, has been entered. Claims 1-12 have been cancelled. Claims 13-28 have been added and are under current examination.

Information Disclosure Statement

Applicants' IDS, filed on 10/31/01 and 3/12/02 have been considered.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 13-28 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, 6, 7, 9-13 of copending Application No. 10/087,142. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of

claims are directed to methods of differentiating pPS cells into cells that have the morphological features of hepatocytes. The instant claims are directed to methods for producing hepatocytes by culturing pPS cells in a medium containing a histone deacteylase inhibitor, and in particular embodiments, n-butyrate. The '142 claims are directed to hepatocyte cell populations and methods of producing the hepatocyte cell populations by culturing pPS cells in the presence of a hepatocyte differentiation factor, in particular n-butyrate. Accordingly, the '142 claims are rendered obvious in view of the instant claims, because they both recite the same methods of differentiating pPS cells in the presence of the same differentiating factor, n-butyrate.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 28 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for producing differentiated cells from pluripotent human ES cells, comprising culturing the human ES cells in a medium containing a histone deacetylase inhibitor, does not reasonably provide

enablement for the methods for producing differentiated cells from human embryonic stem cells in a medium containing a histone deacetylase inhibitor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification teaches methods for generating hepatocytes by differentiating pluripotent primate stem [pPS] cells by culturing the pPS cells in the presence of butyrate or other histone deacetylase inhibitors. The specification teaches that human embryonic stem cells are an example of pPS cells that can be used in the claimed methods. See p. 9, lines 25-32. Although the specification supports that pluripotent human ES cells can be used in the claimed methods, the specification fails to provide sufficient teachings or guidance with regard to the breadth of the claim, which encompasses totipotent, as well as pluripotent, human ES cells. The specification fails to provide teachings or guidance to show that the pPS cells of the instant invention are indeed totipotent, and one of skill in the art would not be able to rely upon the teachings of the art because the art only supports the generation of pluripotent embryonic stem cells. For example, Moreadith *et al.* [J. Mol. Med, 1997], teach that the state of the art is such that ES cell technology is generally limited to the mouse system at present, and that only "putative" ES cells exist for other species. Note that "putative" ES cells lack a demonstration of the cell to give rise to germline tissue or the whole animal, a demonstration which is an art-

recognized property of ES cells. This is further supported by Pera *et al.* [**Journal of Cell Science** 113: 5-10 (2000)] who present the generic criteria for pluripotent ES or EG cells [see p. 6, 2nd column] and state that, "Thus far, only mouse EG or ES cells meet these generic criteria. Primate ES cells meet the first three of the four criteria, but not the last. Numerous other candidate mammalian ES cells have been described over the years in domestic and laboratory species, but only in the mouse have all criteria been met rigorously." [See p. 6, 2nd column, last paragraph].

Accordingly, in view of the specification's lack of teaching or guidance with regard to the breadth of the claims, encompassing totipotent human ES cells, the state of the art of embryonic stem cells, which teach only pluripotent human ES cells, it would have required undue experimentation for one of skill in the art to make and/or use the claimed methods.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 13 is unclear. The claim recites methods for culturing pPS cells or their progeny. It is unclear if "their progeny" refers to undifferentiated pPS cells, or cells that are differentiated from pPS cells (which would also be progeny of pPS cells). Claims 14-26 depend from claim 13. Clarification and/or amendment to the claim is required.

Claim 28 is unclear. The claim recites a method for producing differentiated cells by culturing human ES cells or their progeny. It is unclear if "their progeny" refers to undifferentiated human ES cells, or cells that have been differentiated from the human ES cells. Clarification and/or amendment to the claim is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 27-28 is rejected under 35 U.S.C. 102(b) as being anticipated by Kaneko *et al.* [**Cancer Res.**, 50:3101-3105 (1990), Reference DA of Applicants' IDS filed 3/12/02].

The claim is directed to a method for maintaining cells differentiated from pPS cells [or human embryonic stem cells] comprising culturing the cells in a medium containing a histone deacetylase inhibitor so that at least 60% of the cultured cells meaintain at least three of the following characteristics: antibody-detectable expression of AAT, antibody-detectable expression of albumin, absence of antibody-detectable expression of α-fetoprotein, RT-PCR detectable expression of ASGR, evidence of glycogen storage, cytochrome p450 activity, glucose-6-phosphatase activity; or the morphological features of hepatocytes.

Kaneko teach Chang liver cells, which were established from normal human hepatocytes [see p. 3101, 2nd column, *Materials*] were cultured in butyrate [see p. 3102, 1st column, *Results*, 2nd ¶].

Note that any human cell would be differentiated from pPS cells or human ES, as required by the claims. Furthermore, the claims' requirements of particular characteristics would be inherent to hepatocytes. "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Accordingly Kaneko anticipate the claimed invention.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thaian N. Ton whose telephone number is (571) 272-0736. The Examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time), with alternating Fridays off. Should the Examiner be unavailable, inquiries should be directed to Amy Nelson, Acting SPE of Art Unit 1632, at (571) 272-0804. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

TNT

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Patent Examiner
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